

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
 United States Patent and Trademark
 Office
 Box PCT
 Washington, D.C.20231
 ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 13 July 2000 (13.07.00)	
International application No. PCT/CA99/01123	Applicant's or agent's file reference 42/33984-1
International filing date (day/month/year) 22 November 1999 (22.11.99)	Priority date (day/month/year) 23 November 1998 (23.11.98)
Applicant MILLER, Chris, C.	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

22 June 2000 (22.06.00)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Manu Berrod Telephone No.: (41-22) 338.83.38
---	---

PATENT COOPERATION TREATY

PCT

From the INTERNATIONAL BUREAU

NOTIFICATION RELATING TO PRIORITY CLAIM

(PCT Rules 26bis.1 and 26bis.2 and Administrative Instructions, Sections 402 and 409)

To:

KUHARCHUK, Terr nce, N.
Field Atkins n Perrat n
2000 Oxford Tower
10235 - 101 Street
Edmonton, Alberta T5J 3G1
CANADA

Date of mailing (day/month/year) 20 January 2000 (20.01.00)	
Applicant's or agent's file reference 42/33984-1	IMPORTANT NOTIFICATION
International application No. PCT/CA99/01123	International filing date (day/month/year) 22 November 1999 (22.11.99)
Applicant PULMONOX MEDICAL CORPORATION et al	

The applicant is hereby notified of the following in respect of the priority claim(s) made in the international application.

1. ☒ **Correction of priority claim.** In accordance with the applicant's notice received on: 07 December 1999 (07.12.99), the following priority claim has been corrected to read as follows:
CA 23 November 1998 (23.11.98) 2,254,645.
☐ even though the indication of the number of the earlier application is missing.
☐ even though the following indication in the priority claim is not the same as the corresponding indication appearing in the priority document.

2. ☒ **Addition of priority claim.** In accordance with the applicant's notice received on: the following priority claim has been added:
☐ even though the indication of the number of the earlier application is missing.
☐ even though the following indication in the priority claim is not the same as the corresponding indication appearing in the priority document.

3. ☐ As a result of the correction and/or addition of (a) priority claim(s) under items 1 and/or 2, the (earliest) priority date is:

4. ☒ **Priority claim considered not to have been made.**
☐ The applicant failed to respond to the invitation under Rule 26bis.2(a) (Form PCT/IB/316) within the prescribed time limit.
☐ The applicant's notice was received after the expiration of the prescribed time limit under Rule 26bis.1(a).
☐ The applicant's notice failed to correct the priority claim so as to comply with the requirements of Rule 4.10.
The applicant may, before the technical preparations for international publication have been completed and subject to the payment of a fee, request the International Bureau to publish, together with the international application, information concerning the priority claim. See Rule 26bis.2(c) and the PCT Applicant's Guide, Volume I, Annex B2(IB).

5. ☐ In case where multiple priorities have been claimed, the above item(s) relate to the following priority claim(s):

6. A copy of this notification has been sent to the receiving Office and
☒ to the International Searching Authority (where the international search report has not yet been issued).
☒ the designated Offices (which have already been notified of the receipt of the record copy).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer V. Gross
Facsimile No. (41-22) 740.14.35	Telephone No. (41-22) 338.83.38

PATENT COOPERATION TREATY

PCT

COMMUNICATION IN CASES FOR WHICH
NO OTHER FORM IS APPLICABLE

From the INTERNATIONAL BUREAU

To:

EDWARDS, Antony, C.
206-347 Leon Avenue
Kelowna, British Columbia V1Y 8C2
CANADARECEIVED
MAR - 1 2002
TC 3700 MAIL ROOM

Date of mailing (day/month/year) 31 January 2002 (31.01.02)	REPLY DUE see paragraph 1 below
Applicant's or agent's file reference TE/9264	
International application No. PCT/CA00/01123	International filing date (day/month/year) 28 September 2000 (28.09.00)
Applicant LEMPRIERE, Noel, D.	

1. ☐ REPLY DUE within _____ months/days from the above date of mailing☐ NO REPLY DUE, however, see below☒ IMPORTANT COMMUNICATION☐ INFORMATION ONLY

2. COMMUNICATION:

The applicant in respect of the above identified international application is notified that the receiving Office (RO/CA) has stamped an incorrect international filing date on the first and last pages of the request and has now informed the International Bureau of the corrected date.

Please correct all notifications previously sent by the International Bureau to indicate the correct filing date of:

28 September 2000 (28.09.00)

instead of: **27 September 2000 (27.09.00).**

A copy of this notification has been sent to the receiving Office (RO/CA), the International Searching Authority (ISA/EP) and the designated Offices concerned.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. (41-22) 740.14.35	Authorized officer Céline Faust Telephone No. (41-22) 338.83.38
--	---

PATENT COOPERATION TREATY

From the:
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

KUHARCHUK, TERRENCE N.
Field Atkinson Perraton
2000 Oxford Tower
10235 - 101 Street
Edmonton, Alberta T5J 3G1
CANADA

PCT

RECEIVED

SEP 06 2000 WRITTEN OPINION
FIELD ATKINSON
PERRATON (PCT Rule 66)
and many

Date of mailing
(day/month/year) 29.08.2000

Applicant's or agent's file reference
42/33984-1

REPLY DUE **within 3 month(s)**
from the above date of mailing

International application No.
PCT/CA99/01123

International filing date (day/month/year)
22/11/1999

Priority date (day/month/year)
23/11/1998

International Patent Classification (IPC) or both national classification and IPC
A61K33/08

Applicant

PULMONOX MEDICAL CORPORATION et al.

1. This written opinion is the **first** drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

- I ☒ Basis of the opinion
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain document cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: **23/03/2001**.

Name and mailing address of the international preliminary examining authority:



European Patent Office - P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk - Pays Bas
Tel. +31 70 340 - 2040 Tx: 31 651 epo nl
Fax: +31 70 340 - 3016

Authorized officer / Examiner

Kanbier, D

Formalities officer (incl. extension of time limits)

Sinanovic, E

Telephone No. +31 70 340 2672



WRITTEN OPINION

International application No. PCT/CA99/01123

I. Basis of the opinion

1. This opinion has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed")*:

Description, pages:

1-19 as originally filed

Claims, No.:

1-69 as originally filed

Drawings, sheets:

1/6-6/6 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

- ☐ the entire international application,
☒ claims Nos. 1-69 with respect to industrial applicability,

because:

- ☒ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

s separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the said claims Nos. 1,6-13, 31,36-41.

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 1-11, 14-23, 31-38, 42-51, 56-69
Inventive step (IS)	Claims 1-69
Industrial applicability (IA)	Claims

2. Citations and explanations

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. Claims 1-69 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).
2. An International Search Report was drawn up for the present set of claims, as far as the subject matter included therein is sufficiently defined and supported by (further) claims and by examples, with due regard to the description and the general idea underlying the application.
For subject matter of the present application excluded from the search on this basis, no opinion with regard to novelty and inventive step is included in this preliminary examination.
For a specification of the reasons for possible exclusion of part of the application's subject matter from search and thus from preliminary examination, see Section VIII, point 1. Furthermore, reference is made to the remarks accompanying the International Search Report.

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

For the assessment of the present claims 1-69 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Reference is made to the following documents:

- D1 = WO-A-95 09612 (Entremed Inc.)
- D2 = WO-A-96 31217 (Univ. Duke)
- D3 = US-A-5 632 981 (J.E. Saavedra et al)
- D4 = WO-A-96 00006 (Univ. Pittsburgh)
- D5 = WO-A-96 25184 (Gen. Hosp. Corp.)
- D6 = WO-A-93 17741 (Gen Hosp. Corp.)
- D7 = WO-A-98 01142 (Inst. du N.O. Inc.)

1. The present application does not satisfy the criterion set forth in Article 33(2) PCT because the subject-matter of Claims 1-11, 14-23, 31-38, 42-51 and 56-69 lacks novelty in respect of prior art documents D1-D7 as defined in the regulations (Rule 64(1)-(3) PCT).
 - 1.1 D1 discloses inhibiting the proliferation of infectious and/or pathogenic microorganisms or other proliferating cells in humans or animals, by exposing the m.o. to a compound that releases nitric oxide (NO) in an aqueous solution (claims 1,2,22; page 7, lines 16-18 and 30-32; page 25, lines 16-24). The infectious / pathogenic m.o. are e.g. Mycobacterium tuberculosis, Leishmania and Cryptococcus neoformans, or mediate toxoplasmosis or AIDS (page 30, lines 6-11). Cancers may also be treated in this way (in vivo, localised treatment) (claims 22,23; page 8, lines 31-35). Inhalation devices with NO generators are also envisaged, for treatment of pulmonary infections of viruses, bacteria etc (page 29, lines 14-25; page 23, lines 7-10). Thus D1 anticipates the subject matter of present claims 1-8, 14-23, 31-38, 42-51 and 56-65.
 - 1.2 D2 discloses treatments of a retroviral infection in a cell, tissue or animal so-infected by administration of NO or a NO-delivering, releasing or transferring compound (claims 1,2,15-17; page 2, paragraphs 3-4). Treatment of lung infections by inhalation is envisaged (page 4, paragraph 4; page 16, lines 1-2; page 18, paragraph 3, lines 3-4). The NO in D2 can be gaseous NO or an NO releasing agent (page 6, paragraph 2, lines 1-7). Thus D2 anticipates the subject matter of present claims 1, 6-8, 14, 19-23, 31, 36-38, 42, 47-51, 56 and 61-65.

- 1.3 D3 discloses polymeric compositions capable of releasing NO in physiological conditions, for treating biological disorders in which dosage with NO is beneficial, e.g. in the treatment of tumors, nociception, neurotransmission, etc. The compositions can be incorporated into implants, injectables, condoms, prosthesis coatings, patches, and the like for use in a wide variety of medical applications (column 1, lines 62-63; column 2, lines 45-46; column 3, lines 55-57; column 10, lines 41-54). Dispensing NO from aerosol formulations by inhalation is envisaged (column 11, lines 59-62). Thus D3 anticipates the subject matter of present claims 1, 6-8, 31 and 36-38.
- 1.4 D4 discloses selective induction of NO production with iNOS vectors (as opposed to cNOS, constitutive NO synthase). Induced NO is beneficial in e.g. preventing or combatting microbial infections, such as tuberculosis (page 12, line 26 - page 13, line 14), and treating cancers, when NO is locally induced (page 6, lines 24-26). The iNOS agent can be provided by inhalation to the subject (page 13, lines 27-28; page 37, lines 7-31).
- 1.4.1 Although the present application seems to be directed to exogenous NO as the product of an NO source (page 2, lines 5-6 and page 5, lines 17-27 of the present description), iNOS as NO sources are not excluded thereby. Therefore D4 anticipates the subject matter of present claims 1-5, 14-18, 31-35, 42-46 and 56-60.
- 1.5 D5 discloses the use of gaseous NO for treating arterial restenosis resulting from excessive intimal hyperplasia, i.e. proliferation of arterial smooth muscle cells (claim 1; page 4, lines 10-12), or treating thrombosis e.g. resulting from a disease (page 2, lines 16-28). It is used by inhalation in air or O₂ at concentrations of 0.1-300 ppm, preferably of between 20 and 100 ppm (page 5, lines 24-30; claim 8). Values mentioned and tested are 30, 40, 50, 60 and 80 ppm (page 13, lines 4-10; examples; Table 1; page 34, line 10 - page 35, line 6). Continuous treatment may take place for several days (page 13, lines 19-23).
- 1.5.1 Although no pathogenic cells are involved in the compositions of D5 in the sense of the present application (see Section VIII), they are eminently suitable for use in the treatments presently claimed. Therefore D5 anticipates the subject matter of present claims 56 and 61-69.

- 1.6 D6 discloses a system for producing a mixture comprising NO and air for use in the treatment of medical conditions (pulmonary hypertension etc). The system enables unlimited production at any location of NO, using only air and a source of electricity. The mixture of NO and air is purified and blended with other gases and/or pulmonary therapeutic agents, and the therapeutically effective gas mixture is delivered using organ specific attachments. A portable inhaler provides concentrations of 1-180 ppm NO. In example 2, a level of 40 ppm was used.
- 1.6.1 Although no pathogenic cells are involved in the compositions of D6 in the sense of the present application (see Section VIII), they are eminently suitable for use in the treatments presently claimed. Therefore D6 anticipates the subject matter of present claims 56 and 61-69.
- 1.7 D7 discloses the use of NO as a gaseous drug (page 6, lines 24-27) for preventing or controlling inflammatory response following extracorporeal blood circulation in humans or animals (page 5, lines 15-26). The drug is preferably inhaled and delivered by oral or nasal intubation (page 6, lines 15-16); preferred concentrations range between 0.5-80 ppm or 1-40 ppm (claims 7,8; page 7, lines 6-9). Example 1 discloses 40 ppm.
- 1.7.1 Although no pathogenic cells are involved in the compositions of D7 in the sense of the present application (see Section VIII), they are eminently suitable for use in the treatments presently claimed. Therefore D7 anticipates the subject matter of present claims 56 and 61-69.
2. Even if formal novelty of the above Claims can be reinstated, e.g. by an appropriate amendment, the present application does not satisfy the criterion set forth in Article 33(3) PCT because the subject-matter of Claims 1-69 does not involve an inventive step (Rule 65(1)(2) PCT) in view of D1-D4, separately.
- 2.1 The disclosures of D1-D4 are referred to (points 1.1-1.4 above).
- 2.2 Concerning the dependent claims specifying concentrations of NO in an NO-containing gas, and the time of exposure to such gases, the following is noted: These features are not disclosed specifically in D1-D4, but do not meet the requirements of the PCT in respect of inventive step, as they seem to relate to aspects of common practice in the art. Indeed, optimizing concentrations and treatment times are part of common practice to a skilled person. As long as no

surprising technical effect is achieved thereby (of which there is, in this case, no indication), such features do not render these dependent claims, or any claim to which they refer, inventive.

- 2.3.1 Specific concentrations of NO and exposure times to NO gas falling within the presently claimed ranges are furthermore disclosed in D5, D7 (and D6) which illustrates the fact that these features are in no way surprising to a skilled person.

Re Item VII

Certain defects in the international application

Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in D1-D5 is not mentioned in the description, nor are these documents identified therein.

Re Item VIII

Certain observations on the international application

1. Present claims 1, 6-13, 31 and 36-41 relate to compositions only defined as "pathogenic cells to be suppressed". In view of the description, this definition leads to a lack of clarity within the meaning of Article 6 PCT.
- 1.1 To be able to compare the parameters the applicant has chosen to employ with what is set out in the prior art in the field of the invention, "suppressed pathogenic cells" should have been clearly and comprehensively defined in the description and claims. No comprehensive definition is present in the application. The following passages add to the lack of clarity of the expression "pathogenic cells":
 - (i) Page 1, lines 26-27; page 6, lines 12-14 (pathogenic cells present on medical and other equipment); and
 - (ii) Figures 3-5; pages 16-19; page 1, lines 22-26; page 5, lines 10-15; page 8, line 29 - page 9, line 10; page 9, line 20 - page 10, line 6 (pathogenic cells in any environment to be suppressed by the use of an apparatus as defined in the above parts of the description and figures).

2. It is to be noted that the use of (gaseous) NO for suppressing pathogenic cells, namely viruses, bacteria and other micro-organisms, is known from the prior art. Therefore, introducing the subject matter referred to in 1.1.(i) and (ii) above (in combination with the related embodiments shown e.g. in Figures 1, 4, 5 and described on page 6, lines 12-14) would give rise to a non-unity (Article 34(2) PCT).

For the purpose of examining the present set of claims, this part of the definition of "pathogenic cells" have therefore not been taken into account.

3. Although claims 1, 14, 31, 42 and 56 have been drafted as separate independent claims, they appear to relate effectively to the same subject-matter and to differ from each other only with regard to the definition of the subject-matter for which protection is sought and/or in respect of the terminology used for the features of that subject-matter. The aforementioned claims therefore lack conciseness.
- 3.1 Moreover, lack of clarity of the claims as a whole arises, since the plurality of independent claims makes it difficult to determine the matter for which protection is sought, and places an undue burden on others seeking to establish the extent of the protection. Hence, the above claims do not meet the requirements of Article 6 PCT.
4. The term "about" used in Claims 9-13, 24-29, 39-41, 52-54 and 66-68 is vague and indefinite and as such renders the scope of the claims unclear; accordingly, the claims require amendment to remove this defect (Article 6 PCT).

RECEIVED**PATENT COOPERATION TREATY**WO 00/30659
PCT/CA99/01123JUN 15 2000
FIELD ATKINSON
PERRATON
ENC 1**PCT**

From the INTERNATIONAL BUREAU

To:

KUHARCHUK, Terrence, N.
Field Atkinson Perraton
2000 Oxford Tower
10235 - 101 Street
Edmonton, Alberta T5J 3G1
CANADA**NOTICE INFORMING THE APPLICANT OF THE
COMMUNICATION OF THE INTERNATIONAL
APPLICATION TO THE DESIGNATED OFFICES**

(PCT Rule 47.1(c), first sentence)

Date of mailing (day/month/year) 02 June 2000 (02.06.00)		
Applicant's or agent's file reference 42/33984-1		
IMPORTANT NOTICE		
International application No. PCT/CA99/01123	International filing date (day/month/year) 22 November 1999 (22.11.99)	Priority date (day/month/year) 23 November 1998 (23.11.98)
Applicant PULMONOX MEDICAL CORPORATION et al		

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:
AU,CN,JP,KP,KR,MA,US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:
**AE,AL,AM,AP,AT,AZ,BA,BB,BG,BR,BY,CA,CH,CR,CU,CZ,DE,DK,DM,EA,EE,EP,ES,FI,GB,GD,GE,
GH,GM,HR,HU,ID,IL,IN,IS,KE,KG,KZ,LC,LK,LR,LS,LT,LU,LV,MD,MG,MK,MN,MW,MX,NO,NZ,OA,
PL,PT,RO,RU,SD,SE,SG,SI,SK,SL,TJ,TM,TR,TT,TZ,UA,UG,UZ,VN,YU,ZA,ZW**
The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).
3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on
02 June 2000 (02.06.00) under No. WO 00/30659

REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a demand for international preliminary examination must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the national phase, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO 34, chemin des Colmbettes 1211 GENEVE 20, Switzerland	Authorized officer J. Zahra
Facsimile No. (41-22) 740.14.35	Telephone No. (41-22) 338.83.38

Continuation of Form PCT/IB/308

**NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF
THE INTERNATIONAL APPLICATION TO THE DESIGNATED OFFICES**

Date of mailing (day/month/year) 02 June 2000 (02.06.00)	IMPORTANT NOTICE
Applicant's or agent's file reference 42/33984-1	International application No. PCT/CA99/01123
<p>The applicant is hereby notified that, at the time of establishment of this Notice, the time limit under Rule 46.1 for making amendments under Article 19 has not yet expired and the International Bureau had received neither such amendments nor a declaration that the applicant does not wish to make amendments.</p>	

PATENT COOPERATION TREATY

PCT

From the INTERNATIONAL BUREAU

INFORMATION CONCERNING ELECTED
OFFICES NOTIFIED OF THEIR ELECTION

(PCT Rule 61.3)

To:

KUHARCHUK, Terrence, N.
Field Atkinson Perraton
2000 Oxford Tower
10235 - 101 Street
Edmonton, Alberta T5J 3G1
CANADA

Date of mailing (day/month/year) 13 July 2000 (13.07.00)		
Applicant's or agent's file reference 42/33984-1		IMPORTANT INFORMATION
International application No. PCT/CA99/01123	International filing date (day/month/year) 22 November 1999 (22.11.99)	
		Priority date (day/month/year) 23 November 1998 (23.11.98)
Applicant PULMONOX MEDICAL CORPORATION et al		

1. The applicant is hereby informed that the International Bureau has, according to Article 31(7), notified each of the following Offices of its election:

AP : GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW
EP : AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
National : AU, BG, BR, CA, CN, CZ, DE, IL, JP, KP, KR, MN, NO, NZ, PL, RO, RU, SE, SK, US

2. The following Offices have waived the requirement for the notification of their election; the notification will be sent to them by the International Bureau only upon their request:

EA : AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
OA : BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
National : AE, AL, AM, AT, AZ, BA, BB, BY, CH, CR, CU, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IN, IS, KE, KG, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MW, MX, PT, SD, SG, SI, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW

3. The applicant is reminded that he must enter the "national phase" before the expiration of 30 months from the priority date before each of the Offices listed above. This must be done by paying the national fee(s) and furnishing, if prescribed, a translation of the international application (Article 39(1)(a)), as well as, where applicable, by furnishing a translation of any annexes of the international preliminary examination report (Article 36(3)(b) and Rule 74.1).

Some offices have fixed time limits expiring later than the above-mentioned time limit. For detailed information about the applicable time limits and the acts to be performed upon entry into the national phase before a particular Office, see Volume II of the PCT Applicant's Guide.

The entry into the European regional phase is postponed until 31 months from the priority date for all States designated for the purposes of obtaining a European patent.

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer:

Manu Berrod

Telephone No. (41-22) 338.83.38



The demand must be filed directly with the competent International Preliminary Examining Authority or, if two or more Authorities are competent, with the one chosen by the applicant. The full name or two-letter code of that Authority may be indicated by the applicant on the line below:

IPEA/ EP

PCT

CHAPTER II

DEMAND

under Article 31 of the Patent Cooperation Treaty:
The undersigned requests that the international application specified below be the subject of international preliminary examination according to the Patent Cooperation Treaty and hereby elects all eligible States (except where otherwise indicated).

For International Preliminary Examining Authority use only	
Identification of IPEA	Date of receipt of DEMAND
Box No. I IDENTIFICATION OF THE INTERNATIONAL APPLICATION	
Applicant's or agent's file reference 42/33984-1	
International application No. PCT/CA99/01123	International filing date (day/month/year) 22 November 1999 (22.11.99)
(Earliest) Priority date (day/month/year) 23 November 1998 (23.11.98)	
Title of invention Method and Apparatus For Treatment of Respiratory Infections By Nitric Oxide Inhalation	
Box No. II APPLICANT(S)	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)	
PULMONOX MEDICAL CORPORATION 5243 - 53 Avenue Tofield, Alberta Canada T0B 4J0	
Telephone No.: 1-780-451-2626	
Facsimile No.: 1-780-451-2627	
Teleprinter No.:	
State (that is, country) of nationality: CA	State (that is, country) of residence: CA
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)	
MILLER, Chris C. 4231 Glenhaven Crescent North Vancouver, British Columbia Canada V7G 1B8	
State (that is, country) of nationality: CA	State (that is, country) of residence: CA
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)	
State (that is, country) of nationality:	State (that is, country) of residence:
<input type="checkbox"/> Further applicants are indicated on a continuation sheet.	

Box No. III AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The following person is ☒ agent ☐ common representative
 and ☒ has been appointed earlier and represents the applicant(s) also for international preliminary examination.
☐ is hereby appointed and any earlier appointment of (an) agent(s)/common representative is hereby revoked.
☐ is hereby appointed, specifically for the procedure before the International Preliminary Examining Authority, in addition to the agent(s)/common representative appointed earlier.

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

KUHARCHUK, Terrence N.
 GARWASIUK, Helen
 Field Atkinson Perraton
 2000 Oxford Tower
 10235 - 101 Street
 Edmonton, Alberta Canada T5J 3G1

Telephone No.:

1 - 780 - 423 - 3003

Facsimile No.:

1 - 780 - 428 - 9329

Teleprinter No.:

☐ Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Box No. IV BASIS FOR INTERNATIONAL PRELIMINARY EXAMINATION**Statement concerning amendments: ***

1. The applicant wishes the international preliminary examination to start on the basis of:
 - ☒ the international application as originally filed
 - the description ☐ as originally filed
 - ☐ as amended under Article 34
 - the claims ☐ as originally filed
 - ☐ as amended under Article 19 (together with any accompanying statement)
 - ☐ as amended under Article 34
 - the drawings ☐ as originally filed
 - ☐ as amended under Article 34
 2. ☐ The applicant wishes any amendment to the claims under Article 19 to be considered as reversed.
 3. ☐ The applicant wishes the start of the international preliminary examination to be postponed until the expiration of 20 months from the priority date unless the International Preliminary Examining Authority receives a copy of any amendments made under Article 19 or a notice from the applicant that he does not wish to make such amendments (Rule 69.1(d)). *(This check-box may be marked only where the time limit under Article 19 has not yet expired.)*
- * Where no check-box is marked, international preliminary examination will start on the basis of the international application as originally filed or, where a copy of amendments to the claims under Article 19 and/or amendments of the international application under Article 34 are received by the International Preliminary Examining Authority before it has begun to draw up a written opinion or the international preliminary examination report, as so amended.

Language for the purposes of international preliminary examination: English

- ☒ which is the language in which the international application was filed.
- ☐ which is the language of a translation furnished for the purposes of international search.
- ☐ which is the language of publication of the international application.
- ☐ which is the language of the translation (to be) furnished for the purposes of international preliminary examination.

Box No. V ELECTION OF STATES

The applicant hereby elects all eligible States (that is, all States which have been designated and which are bound by Chapter II of the PCT)

excluding the following States which the applicant wishes not to elect:

Box No. VI CHECK LIST

The demand is accompanied by the following elements, in the language referred to in Box No. IV, for the purposes of international preliminary examination:

- | | | |
|--|---|--------------|
| 1. translation of international application | : | _____ sheets |
| 2. amendments under Article 34 | : | _____ sheets |
| 3. copy (or, where required, translation) of amendments under Article 19 | : | _____ sheets |
| 4. copy (or, where required, translation) of statement under Article 19 | : | _____ sheets |
| 5. letter | : | _____ sheets |
| 6. other (<i>specify</i>) | : | _____ sheets |

For International Preliminary Examining Authority use only

received	not received
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>

The demand is also accompanied by the item(s) marked below:

- | | |
|--|---|
| 1. <input checked="" type="checkbox"/> fee calculation sheet | 4. <input type="checkbox"/> statement explaining lack of signature |
| 2. <input type="checkbox"/> separate signed power of attorney | 5. <input type="checkbox"/> nucleotide and or amino acid sequence listing in computer readable form |
| 3. <input type="checkbox"/> copy of general power of attorney; reference number, if any: | 6. <input type="checkbox"/> other (<i>specify</i>): |

Box No. VII SIGNATURE OF APPLICANT, AGENT OR COMMON REPRESENTATIVE

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the demand).



Helen Garwasiuk
Agent for the Applicants

For International Preliminary Examining Authority use only

1. Date of actual receipt of DEMAND:

2. Adjusted date of receipt of demand due to CORRECTIONS under Rule 60.1(b):

- | | |
|--|---|
| 3. <input type="checkbox"/> The date of receipt of the demand is AFTER the expiration of 19 months from the priority date and item 4 or 5, below, does not apply. | <input type="checkbox"/> The applicant has been informed accordingly. |
| 4. <input type="checkbox"/> The date of receipt of the demand is WITHIN the period of 19 months from the priority date as extended by virtue of Rule 80.5. | |
| 5. <input type="checkbox"/> Although the date of receipt of the demand is after the expiration of 19 months from the priority date, the delay in arrival is EXCUSED pursuant to Rule 82. | |

For International Bureau use only

Demand received from IPEA on:

PCT

CHAPTER II

FEE CALCULATION SHEET

Annex to the Demand for international preliminary examination

<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 30%;">International application No.</td> <td>PCT/CA99/01123</td> </tr> <tr> <td>Applicant's or agent's file reference</td> <td>42/33984-1</td> </tr> </table>	International application No.	PCT/CA99/01123	Applicant's or agent's file reference	42/33984-1	<div style="border: 1px solid black; padding: 5px;"> <p>For International Preliminary Examining Authority use only</p> <p>Date stamp of the IPEA</p> </div>				
International application No.	PCT/CA99/01123								
Applicant's or agent's file reference	42/33984-1								
<p>Applicant</p> <p>PULMONOX MEDICAL CORPORATION et. al.</p>									
<p>Calculation of prescribed fees</p> <p>1. Preliminary examination fee 1533 EUR P</p> <p>2. Handling fee <i>(Applicants from certain States are entitled to a reduction of 75% of the handling fee. Where the applicant is (or all applicants are) so entitled, the amount to be entered at H is 25% of the handling fee.)</i> 147 EUR H</p> <p>3. Total of prescribed fees Add the amounts entered at P and H and enter total in the TOTAL box.....</p> <div style="border: 1px solid black; padding: 5px; text-align: center; width: fit-content; margin: 0 auto;"> <p>1680 EUR</p> <p>TOTAL</p> </div>									
<p>Mode of Payment</p> <table style="width: 100%;"> <tr> <td><input type="checkbox"/> authorization to charge deposit account with the IPEA (see below)</td> <td><input type="checkbox"/> cash</td> </tr> <tr> <td><input type="checkbox"/> cheque</td> <td><input type="checkbox"/> revenue stamps</td> </tr> <tr> <td><input type="checkbox"/> postal money order</td> <td><input type="checkbox"/> coupons</td> </tr> <tr> <td><input checked="" type="checkbox"/> bank draft</td> <td><input type="checkbox"/> other (specify):</td> </tr> </table>		<input type="checkbox"/> authorization to charge deposit account with the IPEA (see below)	<input type="checkbox"/> cash	<input type="checkbox"/> cheque	<input type="checkbox"/> revenue stamps	<input type="checkbox"/> postal money order	<input type="checkbox"/> coupons	<input checked="" type="checkbox"/> bank draft	<input type="checkbox"/> other (specify):
<input type="checkbox"/> authorization to charge deposit account with the IPEA (see below)	<input type="checkbox"/> cash								
<input type="checkbox"/> cheque	<input type="checkbox"/> revenue stamps								
<input type="checkbox"/> postal money order	<input type="checkbox"/> coupons								
<input checked="" type="checkbox"/> bank draft	<input type="checkbox"/> other (specify):								
<p>Deposit Account Authorization <i>(this mode of payment may not be available at all IPEAs)</i></p> <p>The IPEA/ _____ <input type="checkbox"/> is hereby authorized to charge the total fees indicated above to my deposit account.</p> <p><input type="checkbox"/> <i>(this check-box may be marked only if the conditions for deposit accounts of the IPEA so permit)</i> is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated above to my deposit account.</p>									
<p>Deposit Account Number _____</p>	<p>Date (day/month/year) _____</p>								
<p>Signature _____</p>									

PCT REQUEST

42/33984-1

Original (for SUBMISSION) - printed on 22.11.1999 12:53:45 PM

0	For receiving Office use only	
0-1	International Application No.	PCT / CA 99/01123
0-2	International Filing Date	22 NOV 1999 (22.11.99)
0-3	Name of receiving Office and "PCT International Application"	
0-4	Form - PCT/RO/101 PCT Request Prepared using	PCT-EASY Version 2.90 (updated 15.10.1999)
0-5	Petition The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty	
0-6	Receiving Office (specified by the applicant)	Canadian Patent Office (RO/CA)
0-7	Applicant's or agent's file reference	42/33984-1
I	Title of invention	METHOD AND APPARATUS FOR TREATMENT OF RESPIRATORY INFECTIONS BY NITRIC OXIDE INHALATION
II	Applicant	
II-1	This person is:	applicant only
II-2	Applicant for	all designated States except US
II-4	Name	PULMONOX MEDICAL CORPORATION
II-5	Address:	5243 - 53 Avenue Tofield, Alberta T0B 4J0 Canada
II-6	State of nationality	CA
II-7	State of residence	CA
II-8	Telephone No.	1-780-451-2626
II-9	Facsimile No.	1-780-451-2627
III-1	Applicant and/or inventor	
III-1-1	This person is:	applicant and inventor
III-1-2	Applicant for	US only
III-1-4	Name (LAST, First)	MILLER, Chris, C.
III-1-5	Address:	4231 Glenhaven Crescent North Vancouver, British Columbia V7G 1B8 Canada
III-1-6	State of nationality	CA
III-1-7	State of residence	CA

PCT REQUEST

42/33984-1

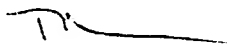
Original (for SUBMISSION) - printed on 22.11.1999 12:53:45 PM

IV-1	Agent or common representative; or - address for correspondence The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as:	agent
IV-1-1	Name (LAST, First)	KUHARCHUK, Terrence, N.
IV-1-2	Address:	FIELD ATKINSON PERRATON 2000 Oxford Tower 10235 - 101 Street Edmonton, Alberta T5J 3G1 Canada
IV-1-3	Telephone No.	1-780-423-7646
IV-1-4	Facsimile No.	1-780-428-9329
IV-1-5	e-mail	tkuharchuk@fielddlaw.com
IV-2	Additional agent(s)	agent
IV-2-1	Name (LAST, First)	GARWASIUK, Helen
IV-2-2	Address:	2000 Oxford Tower 10235 - 101 Street Edmonton, Alberta T5J 3G1 Canada
IV-2-3	Telephone No.	1-780-423-7629
IV-2-4	Facsimile No.	1-780-428-9329
IV-2-5	e-mail	hgarwasiuk@fielddlaw.com
V	Designation of States	
V-1	Regional Patent (other kinds of protection or treatment, if any, are specified between parentheses after the designation(s) concerned)	AP: GH GM KE LS MW SD SL SZ TZ UG ZW and any other State which is a Contracting State of the Harare Protocol and of the PCT EA: AM AZ BY KG KZ MD RU TJ TM and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT EP: AT BE CH&LI CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE and any other State which is a Contracting State of the European Patent Convention and of the PCT OA: BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG and any other State which is a member State of OAPI and a Contracting State of the PCT
V-2	National Patent (other kinds of protection or treatment, if any, are specified between parentheses after the designation(s) concerned)	AE AL AM AT AU AZ BA BB BG BR BY CA CH&LI CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

PCT REQUEST

42/33984-1

Original (for SUBMISSION) - printed on 22.11.1999 12:53:45 PM

V-5	Precautionary Designation Statement In addition to the designations made under items V-1, V-2 and V-3, the applicant also makes under Rule 4.9(b) all designations which would be permitted under the PCT except any designation(s) of the State(s) indicated under item V-6 below. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit.	
V-6	Exclusion(s) from precautionary designations	NONE
VI-1	Priority claim of earlier national application	
VI-1-1	Filing date	23 November 1998 (23.11.1998)
VI-1-2	Number	2,254,545
VI-1-3	Country	CA
VI-2	Priority document request The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) identified above as item(s):	VI-1
VII-1	International Searching Authority Chosen	European Patent Office (EPO) (ISA/EP)
VIII	Check list	
VIII-1	Request	number of sheets: 4 electronic file(s) attached: -
VIII-2	Description	19 -
VIII-3	Claims	7 -
VIII-4	Abstract	1 d004_abstract.txt
VIII-5	Drawings	6 -
VIII-7	TOTAL	37
VIII-8	Accompanying items	
VIII-8	Fee calculation sheet	paper document(s) attached: ✓ electronic file(s) attached: -
VIII-16	PCT-EASY diskette	- diskette
VIII-18	Figure of the drawings which should accompany the abstract	1
VIII-19	Language of filing of the international application	English
IX-1	Signature of applicant or agent	
IX-1-1	Name (LAST, First)	KUHARCHUK, Terrence, N.

FOR RECEIVING OFFICE USE ONLY

10-1	Date of actual receipt of the purported international application	22 Nov 1999 (22.11.99)
------	---	------------------------

PCT REQUEST

42/33984-1

Original (for SUBMISSION) - printed on 22.11.1999 12:53:45 PM

10-2	Drawings:	
10-2-1	Received ✓	
10-2-2	Not received	
10-3	Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application	
10-4	Date of timely receipt of the required corrections under PCT Article 11(2)	
10-5	International Searching Authority	ISA/EP
10-6	Transmittal of search copy delayed until search fee is paid	

FOR INTERNATIONAL BUREAU USE ONLY

11-1	Date of receipt of the record copy by the International Bureau	
------	--	--

PCT (ANNEX - FEE CALCULATION SHEET)

42/33984-1

Original (for SUBMISSION) - printed on 22.11.1999 12:53:45 PM

(This sheet is not part of and does not count as a sheet of the international application)

0	For receiving Office use only	
0-1	International Application No.	PCT / CA 99 / 01123
0-2	Date stamp of the receiving Office	22 NOV 1999 (22 11 99)
0-4	Form - PCT/RO/101 (Annex) PCT Fee Calculation Sheet	
0-4-1	Prepared using	PCT-EASY Version 2.90 (updated 15.10.1999)
0-9	Applicant's or agent's file reference	42/33984-1
2	Applicant	PULMONOX MEDICAL CORPORATION, et al.
12	Calculation of prescribed fees	fee amount/multiplier total amounts (CAD)
12-1	Transmittal fee T	⇒ 200
12-2	Search fee S	⇒ 1,874
12-3	International fee	
	Basic fee (first 30 sheets) b1	641
12-4	Remaining sheets	7
12-5	Additional amount (X)	15
12-6	Total additional amount b2	105
12-7	b1 + b2 = B	746
12-8	Designation fees	
	Number of designations contained in international application	83
12-9	Number of designation fees payable (maximum 10)	10
12-10	Amount of designation fee (X)	148
12-11	Total designation fees D	1,480
12-12	PCT-EASY fee reduction R	-197
12-13	Total International fee (B+D-R) I	⇒ 2,029
12-14	Fee for priority document	
	Number of priority documents requested	1
12-15	Fee per document (X)	46.5
12-16	Total priority document fee P	⇒ 46.5
12-17	TOTAL FEES PAYABLE (T+S+I+P)	⇒ 4,149.5
12-19	Mode of payment	other: Fee for certified copy of priority document enclosed, other fees not enclosed at this time

VALIDATION LOG AND REMARKS

PCT (ANNEX - FEE CALCULATION SHEET)

42/33984-1

Original (for SUBMISSION) - printed on 22.11.1999 12:53:45 PM

13-2-6	Validation messages Contents	Yellow! The power of attorney or a copy of the general power of attorney will need to be furnished unless all applicants sign the request form.
13-2-7	Validation messages Fees	Green? Please verify that modified fee amounts are correct.

PATENT COOPERATION TREATY

From the RECEIVING OFFICE

To: KUHARCHUK, TERRENCE N. FIELD ATKINSON PERRATON 2000 Oxford Tower 10235 - 101 Street Edmonton, Alberta T5J 3G1 Canada	<h2 style="margin: 0;">PCT</h2> <p style="margin: 5px 0 0 0;">NOTIFICATION RELATING TO PRIORITY CLAIM</p> <p style="margin: 5px 0 0 40px;">(PCT Rules 26bis.1 and 26bis.2 and Administrative Instructions, Sections 302 and 314)</p>
Applicant's or agent's file reference 42/33984-1	Date of mailing (day/month/year) 24 December 1999 (24.12.1999)
International application No. PCT/CA99/01123	International filing date (day/month/year) 22 November 1999 (22-11-99)
Applicant PULMONOX MEDICAL CORPORATION ET AL	

The applicant is hereby **notified** of the following in respect of the priority claim(s) made in the international application.

1. ☒ **Correction of priority claim.** In accordance with the applicant's notice received on: 07 December 1999 the following priority claim has been corrected to read as follows: should be 2,254,645 instead of 2,254,545
 - ☐ even though the indication of the number of the earlier application is missing.
 - ☐ even though the following indication in the priority claim is not the same as the corresponding indication appearing in the priority document:

2. ☐ **Addition of priority claim.** In accordance with the applicant's notice received on: _____ the following priority claim has been added:
 - ☐ even though the indication of the number of the earlier application is missing.
 - ☐ even though the following indication in the priority claim is not the same as the corresponding indication appearing in the priority document:

3. ☐ **As a result of the correction and/or addition** of (a) priority claim(s) under items 1 and/or 2, the **(earliest) priority date** is:

4. ☐ The priority claim (*see also item 5, below, if applicable*) **is considered not to have been made** because:
 - ☐ the applicant failed to respond to the invitation under Rule 26bis.2(a) (Form PCT/RO/110) within the prescribed time limit.
 - ☐ the applicant's notice was received after the expiration of the prescribed time limit under Rule 26bis.1(a).
 - ☐ the applicant's notice failed to correct the priority claim so as to comply with the requirements of Rule 4.10.

The applicant may, before the technical preparations for international publication have been completed and subject to the payment of a fee, request the International Bureau to publish, together with the international application, information concerning the priority claim. See Rule 26bis.2(c) and the *PCT Applicant's Guide*, Volume I, Annex B2(IB).

5. ☐ In case where **multiple priorities** have been claimed, the above item(s) relate to the following priority claim(s):

6. A copy of this notification has been sent to the International Bureau and
☒ to the International Searching Authority

Name and mailing address of the Receiving Office Commissioner of Patents Canadian Receiving Office Box PCT, Ottawa/Hull K1A 0C9 Facsimile No. (819) 953-9538	Authorized Officer <i>Carole Millaire</i> Carole Millaire (819) 994-6587 Telephone No. (819) 953-9712
--	---

PATENT COOPERATION TREATY

PCT

From the INTERNATIONAL BUREAU

NOTIFICATION CONCERNING
SUBMISSION OR TRANSMITTAL
OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

To:

KUHARCHUK, Terrence, N.
Field Atkinson Perraton
2000 Oxford Tower
10235 - 101 Street
Edmonton, Alberta T5J 3G1
CANADA

Date of mailing (day/month/year) 20 January 2000 (20.01.00)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference 42/33984-1	
International application No. PCT/CA99/01123	International filing date (day/month/year) 22 November 1999 (22.11.99)
International publication date (day/month/year) Not yet published	Priority date (day/month/year) 23 November 1998 (23.11.98)
Applicant PULMONOX MEDICAL CORPORATION et al	

1. The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).
2. This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.
3. An asterisk(*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.
4. The letters "NR" appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

<u>Priority date</u>	<u>Priority application No.</u>	<u>Country or regional Office or PCT receiving Office</u>	<u>Date of receipt of priority document</u>
23 Nove 1998 (23.11.98)	2,254,645	CA	17 Dec 1999 (17.12.99)

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. (41-22) 740.14.35	Authorized officer V. Gross Telephone No. (41-22) 338.83.38
--	---

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

14

Applicant's or agent's file reference 42/33984-1	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/CA99/01123	International filing date (day/month/year) 22/11/1999	Priority date (day/month/year) 23/11/1998
International Patent Classification (IPC) or national classification and IPC A61K33/08		
Applicant PULMONOX MEDICAL CORPORATION et al.		

- This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
- This REPORT consists of a total of 10 sheets, including this cover sheet.
 - ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims, and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.



- This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

RECEIVED

MAY 11 2001

TECHNOLOGY CENTER R3700

Date of submission of the demand 22/06/2000	Date of completion of this report 16.03.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized officer Kanbier, D Telephone No. +31 70 340 3465 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/CA99/01123

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).)*:

Description, pages:

1-19 as originally filed

Claims, No.:

1-69 as originally filed

Drawings, sheets:

1/6-6/6 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/CA99/01123

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. 1-55 with respect to industrial applicability.

because:

- ☒ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the said claims Nos. 1,6-13, 31,36-41.

2. A meaningful international preliminary examination report cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.
- ☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N) Yes: Claims

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/CA99/01123

	No:	Claims	1-11, 14-23, 31-38, 42-51, 56-69
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-69
Industrial applicability (IA)	Yes:	Claims	See separate sheet
	No:	Claims	

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/CA99/01123

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. Claims 1-55 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).
2. An International Search Report was drawn up for the present set of claims, as far as the subject matter included therein is sufficiently defined and supported by (further) claims and by examples, with due regard to the description and the general idea underlying the application.
For subject matter of the present application excluded from the search on this basis, no opinion with regard to novelty and inventive step is included in this preliminary examination.
For a specification of the reasons for possible exclusion of part of the application's subject matter from search and thus from preliminary examination, see Section VIII, point 1. Furthermore, reference is made of the remarks accompanying the International Search Report.

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

For the assessment of the present claims 56-69 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/CA99/01123

Reference is made to the following documents:

- D1 = WO-A-95 09612 (Entremed Inc.)
- D2 = WO-A-96 31217 (Univ. Duke)
- D3 = US-A-5 632 981 (J.E. Saavedra et al)
- D4 = WO-A-96 00006 (Univ. Pittsburgh)
- D5 = WO-A-96 25184 (Gen. Hosp. Corp.)
- D6 = WO-A-93 17741 (Gen Hosp. Corp.)
- D7 = WO-A-98 01142 (Inst. du N.O. Inc.)

1. The present application does not satisfy the criterion set forth in Article 33(2) PCT because the subject-matter of Claims 1-11, 14-23, 31-38, 42-51 and 56-69 lacks novelty in respect of prior art documents D1-D7 as defined in the regulations (Rule 64(1)-(3) PCT).

1.1 D1 discloses inhibiting the proliferation of infectious and/or pathogenic microorganisms or other proliferating cells in humans or animals, by exposing the m.o. to a compound that releases nitric oxide (NO) in an aqueous solution (claims 1, 2, 22; page 7, lines 16-18 and 30-32; page 25, lines 16-24). The infectious / pathogenic m.o. are e.g. Mycobacterium tuberculosis, Leishmania and Cryptococcus neoformans, or mediate toxoplasmosis or AIDS (page 30, lines 6-11). Cancers may also be treated in this way (in vivo, localised treatment) (claims 22, 23; page 8, lines 31-35). Inhalation devices with NO generators are also envisaged, for treatment of pulmonary infections of viruses, bacteria etc (page 29, lines 14-25; page 23, lines 7-10). Thus D1 anticipates the subject matter of present claims 1-8, 14-23, 31-38, 42-51 and 56-65.

1.2 D2 discloses treatments of a retroviral infection in a cell, tissue or animal so-infected by administration of NO or a NO-delivering, releasing or transferring compound (claims 1,2,15-17; page 2, paragraphs 3-4). Treatment of lung infections by inhalation is envisaged (page 4, paragraph 4; page 16, lines 1-2; page 18, paragraph 3, lines 3-4). The NO in D2 can be gaseous NO or an NO releasing agent (page 6, paragraph 2, lines 1-7). Thus D2 anticipates the subject matter of present claims 1, 6-8, 14, 19-23, 31, 36-38, 42, 47-51, 56 and 61-65.

- 1.3 D3 discloses polymeric compositions capable of releasing NO in physiological conditions, for treating biological disorders in which dosage with NO is beneficial, e.g. in the treatment of tumors, nociception, neurotransmission, etc. The compositions can be incorporated into implants, injectables, condoms, prosthesis coatings, patches, and the like for use in a wide variety of medical applications (column 1, lines 62-63; column 2, lines 45-46; column 3, lines 55-57; column 10, lines 41-54). Dispensing NO from aerosol formulations by inhalation is envisaged (column 11, lines 59-62). Thus D3 anticipates the subject matter of present claims 1, 6-8, 31 and 36-38.
- 1.4 D4 discloses selective induction of NO production with iNOS vectors (as opposed to cNOS, constitutive NO synthase). Induced NO is beneficial in e.g. preventing or combatting microbial infections, such as tuberculosis (page 12, line 26 - page 13, line 14), and treating cancers, when NO is locally induced (page 6, lines 24-26). The iNOS agent can be provided by inhalation to the subject (page 13, lines 27- 28; page 37, lines 7-31).
- 1.4.1 Although the present application seems to be directed to exogenous NO as the product of an NO source (page 2, lines 5-6 and page 5, lines 17-27 of the present description), iNOS as NO sources are not excluded thereby. Therefore D4 anticipates the subject matter of present claims 1-5, 14-18, 31-35, 42-46 and 56-60.
- 1.5 D5 discloses the use of gaseous NO for treating arterial restenosis resulting from excessive intimal hyperplasia, i.e. proliferation of arterial smooth muscle cells (claim 1; page 4, lines 10-12), or treating thrombosis e.g. resulting from a disease (page 2, lines 16-28). It is used by inhalation in air or O₂ at concentrations of 0.1-300 ppm, preferably of between 20 and 100 ppm (page 5, lines 24-30; claim 8). Values mentioned and tested are 30, 40, 50, 60 and 80 ppm (page 13, lines 4- 10; examples; Table 1; page 34, line 10 - page 35, line 6). Continuous treatment may take place for several days (page 13, lines 19-23).
- 1.5.1 Although no pathogenic cells are involved in the compositions of D5 in the sense of the present application (see Section VIII), they are eminently suitable for use in the treatments presently claimed. Therefore D5 anticipates the subject matter of present claims 56 and 61-69.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/CA99/01123

- 1.6 D6 discloses a system for producing a mixture comprising NO and air for use in the treatment of medical conditions (pulmonary hypertension etc). The system enables unlimited production at any location of NO, using only air and a source of electricity. The mixture of NO and air is purified and blended with other gases and/or pulmonary therapeutic agents, and the therapeutically effective gas mixture is delivered using organ specific attachments. A portable inhaler provides concentrations of 1-180 ppm NO. In example 2, a level of 40 ppm was used.
- 1.6.1 Although no pathogenic cells are involved in the compositions of D6 in the sense of the present application (see Section VIII), they are eminently suitable for use in the treatments presently claimed. Therefore D6 anticipates the subject matter of present claims 56 and 61-69.
- 1.7 D7 discloses the use of NO as a gaseous drug (page 6, lines 24-27) for preventing or controlling inflammatory response following extracorporeal blood circulation in humans or animals (page 5, lines 15-26). The drug is preferably inhaled and delivered by oral or nasal intubation (page 6, lines 15-16); preferred concentrations range between 0.5-80 ppm or 1-40 ppm (claims 7,8; page 7, lines 6-9). Example 1 discloses 40 ppm.
- 1.7.1 Although no pathogenic cells are involved in the compositions of D7 in the sense of the present application (see Section VIII), they are eminently suitable for use in the treatments presently claimed. Therefore D7 anticipates the subject matter of present claims 56 and 61-69.
- 2. The present application also does not satisfy the criterion set forth in Article 33(3) PCT because the subject-matter of Claims 1-69 does not involve an inventive step (Rule 65(1)(2) PCT) in view of D1-D4, separately.
- 2.1 The disclosures of D1-D4 are referred to (points 1.1-1.4 above).
- 2.2 Concerning the dependent claims specifying concentrations of NO in an NO-containing gas, and the time of exposure to such gases, the following is noted:

These features are not disclosed specifically in D1-D4, but do not meet the requirements of the PCT in respect of inventive step, as they seem to relate to aspects of common practice in the art. Indeed, optimizing concentrations and treatment times are part of common practice to a skilled person. As long as no surprising technical effect is achieved thereby (of which there is, in this case, no indication), such features do not render these dependent claims, or any claim to which they refer, inventive.

- 2.3.1 Specific concentrations of NO and exposure times to NO gas falling within the presently claimed ranges are furthermore disclosed in D5, D7 (and D6) which illustrates the fact that these features are in no way surprising to a skilled person.

Re Item VII

Certain defects in the international application

Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in D1-D5 is not mentioned in the description, nor are these documents identified therein.

Re Item VIII

Certain observations on the international application

1. Present claims 1, 6-13, 31 and 36-41 relate to compositions only defined as "pathogenic cells to be suppressed". In view of the description, this definition leads to a lack of clarity within the meaning of Article 6 PCT.
- 1.1 To be able to compare the parameters the applicant has chosen to employ with what is set out in the prior art in the field of the invention, "suppressed pathogenic cells" should have been clearly and comprehensively defined in the description and claims. No comprehensive definition is present in the application. The following passages add to the lack of clarity of the expression "pathogenic cells":
- (i) Page 1, lines 26-27; page 6, lines 12-14 (pathogenic cells present on medical and other equipment); and

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/CA99/01123

- (ii) Figures 3-5; pages 16-19; page 1, lines 22-26; page 5, lines 10-15; page 8, line 29 - page 9, line 10; page 9, line 20 - page 10, line 6 (pathogenic cells in any environment to be suppressed by the use of an apparatus as defined in the above parts of the description and figures).

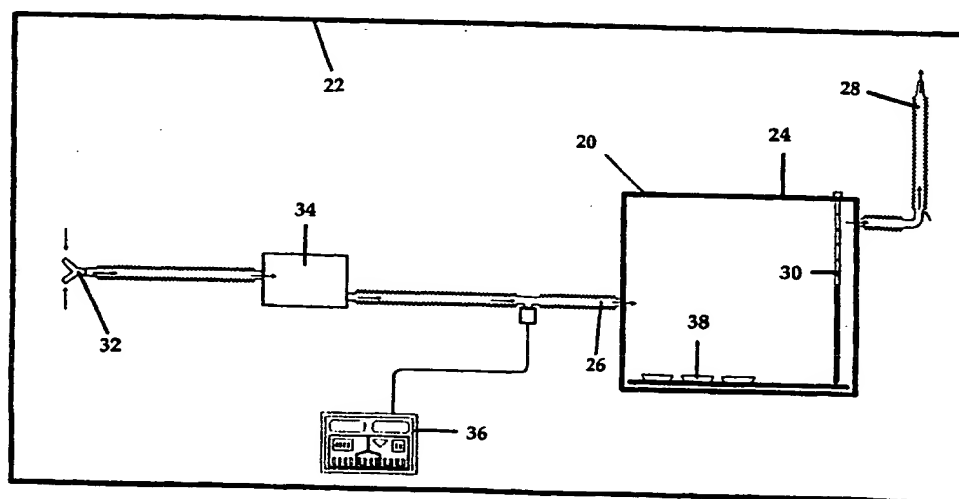
2. Although claims 1, 14, 31, 42 and 56 have been drafted as separate independent claims, they appear to relate effectively to the same subject-matter and to differ from each other only with regard to the definition of the subject-matter for which protection is sought and/or in respect of the terminology used for the features of that subject-matter. The aforementioned claims therefore lack conciseness.
- 2.1 Moreover, lack of clarity of the claims as a whole arises, since the plurality of independent claims makes it difficult to determine the matter for which protection is sought, and places an undue burden on others seeking to establish the extent of the protection. Hence, the above claims do not meet the requirements of Article 6 PCT.
3. The term "about" used in Claims 9-13, 24-29, 39-41, 52-54 and 66-68 is vague and indefinite and as such renders the scope of the claims unclear (Article 6 PCT).



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ : A61K 33/08, A61M 15/00, A61L 2/00		A1	(11) International Publication Number: WO 00/30659
			(43) International Publication Date: 2 June 2000 (02.06.00)
(21) International Application Number: PCT/CA99/01123		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).	
(22) International Filing Date: 22 November 1999 (22.11.99)			
(30) Priority Data: 2,254,645 23 November 1998 (23.11.98) CA			
(71) Applicant (for all designated States except US): PULMONOX MEDICAL CORPORATION [CA/CA]; 5243 - 53 Avenue, Tofield, Alberta T0B 4J0 (CA).			
(72) Inventor; and (75) Inventor/Applicant (for US only): MILLER, Chris, C. [CA/CA]; 4231 Glenhaven Crescent, North Vancouver, British Columbia V7G 1B8 (CA).			
(74) Agents: KUHARCHUK, Terrence, N. et al.; Field Atkinson Perraton, 2000 Oxford Tower, 10235 - 101 Street, Edmonton, Alberta T5J 3G1 (CA).		Published With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.	

(54) Title: METHOD AND APPARATUS FOR TREATMENT OF RESPIRATORY INFECTIONS BY NITRIC OXIDE INHALATION



(57) Abstract

The invention relates to a method for suppressing pathogenic cells and a method for the treatment of an animal, including a human, having pathogenic cells within its respiratory tract. These methods preferably comprise the exposure of the pathogenic cells to an effective amount of a source of nitric oxide, the nitric oxide source comprising nitric oxide or a compound or substance capable of producing nitric oxide and wherein the nitric oxide may have either an inhibitory or a cidal effect on such pathogenic cells. Further, the invention relates to the use of nitric oxide for suppressing pathogenic cells, the therapeutic use of nitric oxide for the treatment of an animal having pathogenic cells in its respiratory tract and a pharmaceutical composition for such treatment.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
CM	Cameroon			PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakhstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 99/01123

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K33/08 A61M15/00 A61L2/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WO 95 09612 A (ENTREMED INC) 13 April 1995 (1995-04-13)</p> <p>page 5, line 6-13; claims 1,2,22,23 page 7, line 13-18 page 7, line 30-34 page 8, line 20-35 page 23, line 7-13 page 25, line 16-24 page 29, line 14-25 page 30, line 6-11</p> <p style="text-align: center;">-/-</p>	<p>1-8, 14-23, 31-38, 42-51, 56-65</p>

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

18 April 2000

Date of mailing of the international search report

27/04/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax (+31-70) 340-3016

Authorized officer

Kanbier, D

INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 99/01123

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WO 96 31217 A (UNIV DUKE) 10 October 1996 (1996-10-10)</p> <p>page 2, paragraphs 3,4 page 16, line 1,2 page 18, paragraph 3; claims 1,2,15-17 page 6-10 page 4, paragraph 4</p>	<p>1,6-8, 14, 19-23, 31, 36-38, 42, 47-51, 56,61-65</p>
X	<p>US 5 632 981 A (SAAVEDRA JOSEPH E ET AL) 27 May 1997 (1997-05-27) column 11, line 59-65 column 1, line 62-65</p>	<p>1,6-8, 31,36-38</p>
X	<p>WO 96 00006 A (UNIV PITTSBURGH) 4 January 1996 (1996-01-04)</p> <p>page 5, line 15-21; claims 1,2 page 12, line 26 -page 13, line 28 page 3, line 14-19 page 6, line 24-26 page 36, line 6 -page 38, line 5 page 50, line 15-28</p>	<p>1-5, 14-18, 31-35, 42-46, 56-60</p>
X A	<p>WO 96 25184 A (GEN HOSPITAL CORP) 22 August 1996 (1996-08-22) page 2, line 16-28</p> <p>page 4, line 10-12; claims 1,8 page 5, line 24-30; tables page 13, line 4-10 page 13, line 19-23; figure 4 page 34, line 10 -page 35, line 6</p>	<p>56,61-69</p> <p>1,6-11, 14, 19-27, 31, 36-42, 47-55</p>
X A	<p>WO 93 17741 A (GEN HOSPITAL CORP) 16 September 1993 (1993-09-16) page 5, line 2-14; figures; example 2 page 7, line 4-21; claims 1,6,7,10 page 10, line 34 -page 11, line 2</p>	<p>56,61-69</p> <p>1,6-11, 14, 19-27, 31, 36-42, 47-55</p>
	-/-	

INTERNATIONAL SEARCH REPORT

Inte onal Application No

PCT/CA 99/01123

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 01142 A (INST DU N.O. INC) 15 January 1998 (1998-01-15) page 5, line 15-26; example 1	56, 61-69
A	page 6, line 15-27; claims 1, 3-8, 11 page 7, line 6-9	1, 6-11, 14, 19-27, 31, 36-42, 47-55

INTERNATIONAL SEARCH REPORT

International application No.

PCT/CA 99/01123

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claim(s) 1-69
is(are) directed to a method of treatment of the human/animal
body, the search has been carried out and based on the alleged
effects of the compound/composition.
2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such
an extent that no meaningful International Search can be carried out, specifically:
SEE FURTHER INFORMATION SHEET PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all
searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment
of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report
covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is
restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 1, 6-13, 31 and 36-41 relate to objects of treatment only defined as "pathogenic cells to be suppressed". In view of the description, this definition could lead to a lack of clarity within the meaning of Article 6 PCT.

To be able to compare the parameters the applicant has chosen to employ with what is set out in the prior art in the field of the invention, the search has been restricted to "suppressed pathogenic cells" as defined in the description and claims, except for the claims mentioned above and the following parts of the description:

Page 1, lines 22-27; page 6, lines 12-14 (pathogenic cells present on medical and other equipment).

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

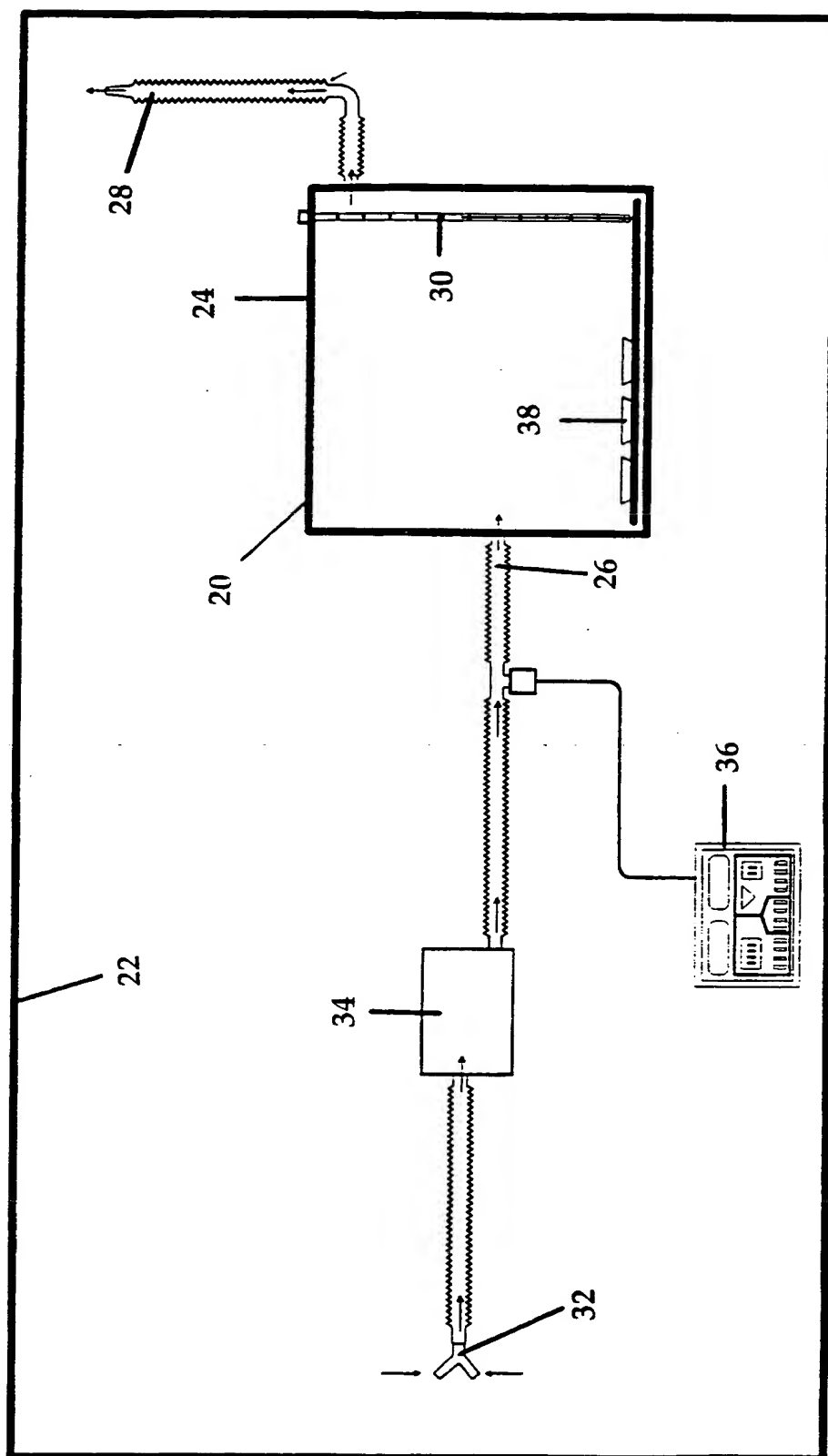
INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/CA 99/01123

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9509612 A	13-04-1995	AU 7972294 A US 5814666 A	01-05-1995 29-09-1998
WO 9631217 A	10-10-1996	AU 5527196 A	23-10-1996
US 5632981 A	27-05-1997	US 5525357 A US 5405919 A AU 4286496 A EP 0793500 A JP 10510249 T WO 9615797 A US 5650447 A US 5910316 A US 5718892 A US 5676963 A US 5691423 A	11-06-1996 11-04-1995 17-06-1996 10-09-1997 06-10-1998 30-05-1996 22-07-1997 08-06-1999 17-02-1998 14-10-1997 25-11-1997
WO 9600006 A	04-01-1996	US 5658565 A AU 716623 B AU 2869095 A CA 2193827 A EP 0769903 A JP 10501989 T US 5830461 A ZA 9505210 A	19-08-1997 02-03-2000 19-01-1996 04-01-1996 02-05-1997 24-02-1998 03-11-1998 21-02-1996
WO 9625184 A	22-08-1996	AU 690425 B AU 4777596 A BR 9607616 A CA 2213188 A CN 1174513 A CZ 9702598 A EP 0810884 A FI 973357 A JP 11500125 T NO 973768 A US 5904938 A ZA 9601183 A	23-04-1998 04-09-1996 09-06-1998 22-08-1996 25-02-1998 13-05-1998 10-12-1997 15-08-1997 06-01-1999 15-10-1997 18-05-1999 17-12-1996
WO 9317741 A	16-09-1993	US 5396882 A BR 9306060 A CA 2117691 A EP 0630270 A FI 944170 A JP 7505073 T MX 9301357 A NO 943349 A US 5536241 A	14-03-1995 18-11-1997 16-09-1993 28-12-1994 09-09-1994 08-06-1995 29-04-1994 10-11-1994 16-07-1996
WO 9801142 A	15-01-1998	CA 2180506 A AU 3086097 A EP 0910391 A	05-01-1998 02-02-1998 28-04-1999

Figure 1

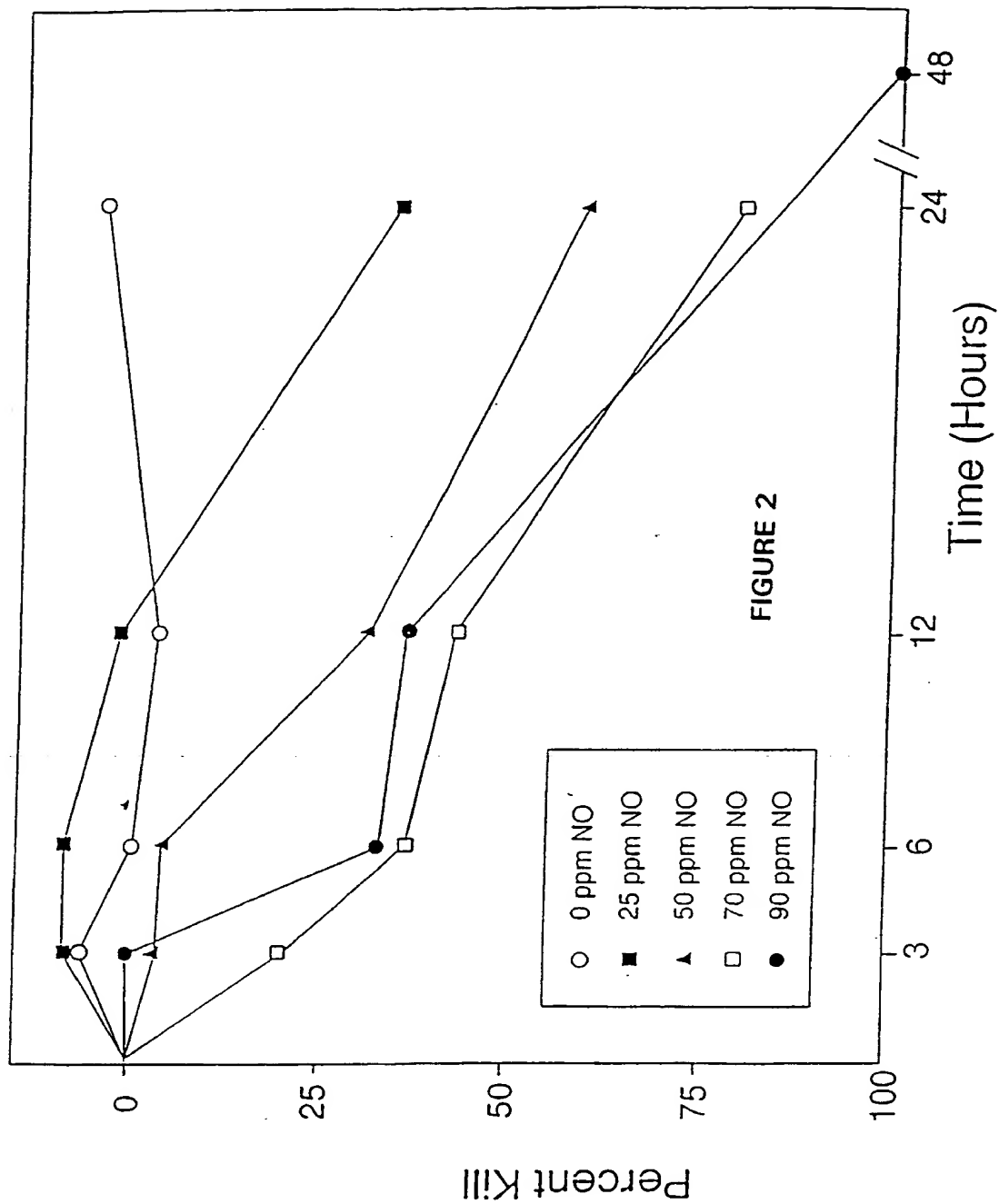
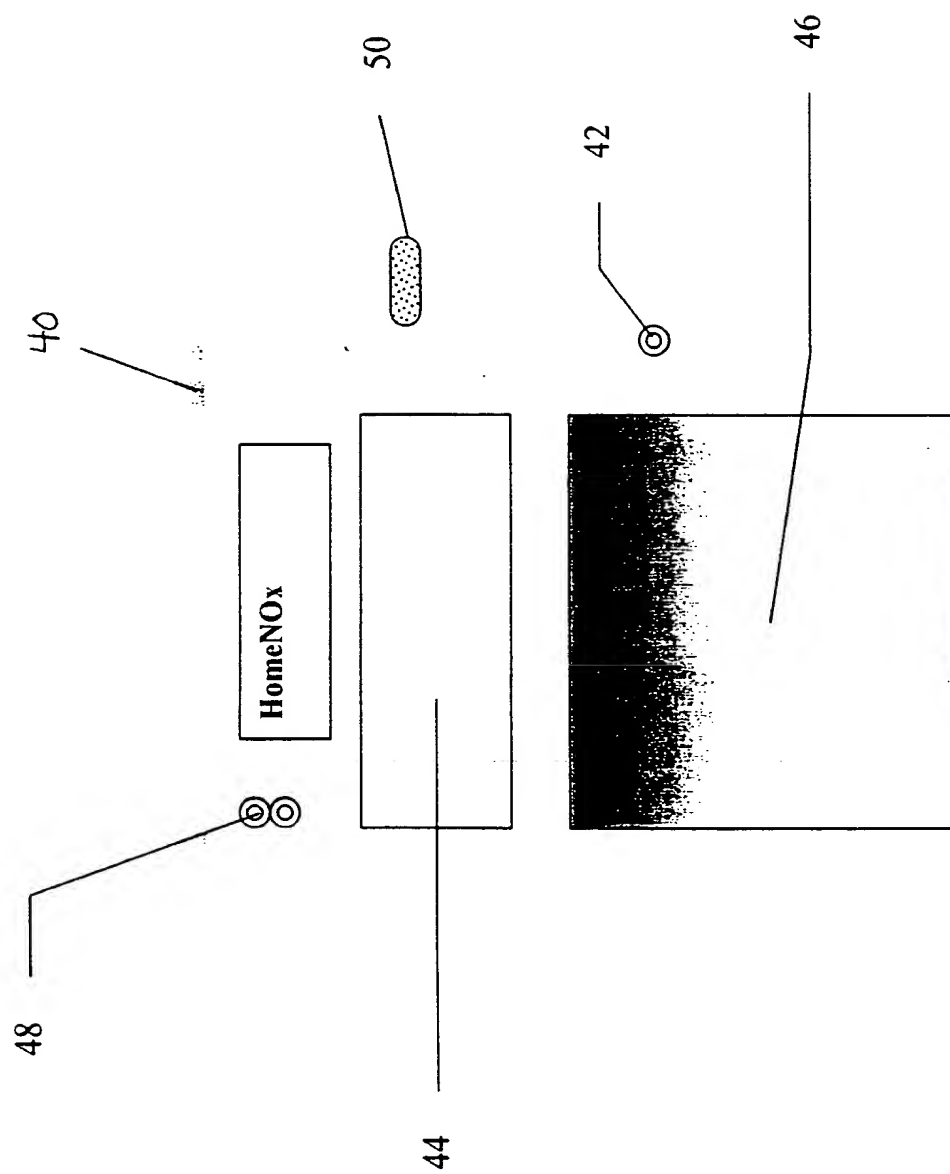


Figure 3a



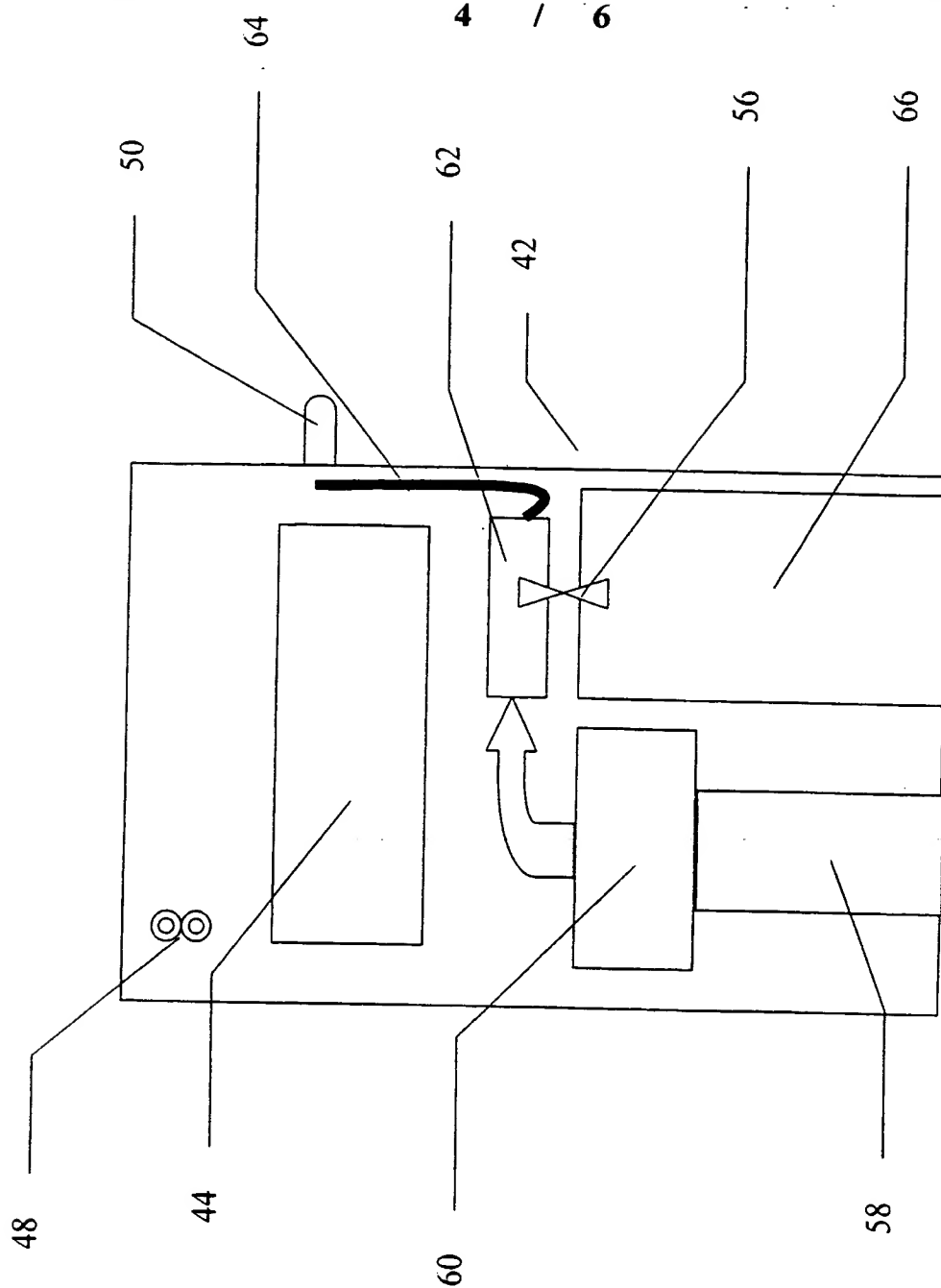


Figure 3b

Figure 5

